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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,959	08/16/2005	Chaim Gilon	28557	7550

7590 04/05/2007

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EXAMINER	
DESAI, ANAND U	
ART UNIT	**PAPER NUMBER**
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,959	GILON ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2006*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-131* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-9, 15-17, 25-33, 34, and 40-42, drawn to a conjugate comprising a histone moiety covalently linked to a protein.

Group II, claim(s) 1-8, 10-14, 15-17, 25-33, 35-39, and 40-42, drawn to a conjugate comprising a histone moiety covalently linked to a nucleic acid.

Group III, claim(s) 18-24, drawn to a polynucleotide encoding an in-frame polypeptide conjugate, said polypeptide conjugate comprises a histone moiety and a protein-of-interest.

Group IV, claim(s) 43-60, 61, 67, and 68, drawn to a method of synthesizing a conjugate comprising a histone moiety with a protein, comprising covalently linking a histone moiety with a protein.

Group V, claim(s) 43-60, 62-66, 67, and 68, drawn to a method of synthesizing a conjugate comprising a histone moiety with a nucleic acid.

Group VI, claim(s) 69-77, 78, and 84-86, drawn to a method of delivering a protein into a cell, comprising contacting the cell with a protein conjugate.

Group VII, claim(s) 69-77, 79-83, and 84-86, drawn to a method of delivering a nucleic acid into a cell, comprising contacting the cell with a conjugate comprising a nucleic acid.

Group VIII, claim(s) 87-92, 93, and 99-101, drawn to a method of treating a proliferative disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a proliferative disorder or disease.

Group IX, claim(s) 87-92, 93, and 99-101, drawn to a method of treating a genetic disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a genetic disorder or disease.

Group X, claim(s) 87-92, 93, and 99-101, drawn to a method of treating a bacterial infection in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a bacterial infection.

Group XI, claim(s) 87-92, 93, and 99-101, drawn to a method of treating a viral infection in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a viral infection.

Group XII, claim(s) 87-92, 94-98, and 99-101, drawn to a method of treating a proliferative disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a proliferative disorder or disease.

Group XIII, claim(s) 87-92, 94-98, and 99-101, drawn to a method of treating a genetic disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a genetic disorder or disease.

Group XIV, claim(s) 87-92, 94-98, and 99-101, drawn to a method of treating a bacterial infection in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a bacterial infection.

Group XV, claim(s) 87-92, 94-98, and 99-101, drawn to a method of treating a viral infection in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a viral infection.

Group XVI, claim(s) 102-110, 111, 113-116, 117, and 118, drawn to a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a protein into cells.

Group XVII, claim(s) 102-110, 112, 117, 118, and 119-122, drawn to a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a nucleic acid into cells.

Group XVIII, claim(s) 102, 123, 124, and 125-127, drawn to a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a conjugate of a first macromolecule covalently attached to a second macromolecule, wherein the first macromolecule is a histone moiety, and the second macromolecule is a protein.

Group XIX, claim(s) 102, 123, 124, 125-127, and 128-131, drawn to a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a conjugate of a first

macromolecule covalently attached to a second macromolecule, wherein the first macromolecule is a histone moiety, and the second macromolecule is a nucleic acid.

2. The inventions listed as Groups I-XIX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the technical feature linking the composition claims appears to be that they all relate to a conjugate comprising a histone moiety covalently linked to a macromolecule-of-interest. However, Plaue et al. (U.S. Patent 5,545,718) describes a conjugate of a heat-shock protein, ubiquitine, containing 76 amino acid residues with histones by means of a peptide bond between the group α-COOH of the C-terminal glycine in position 76 of the ubiquitine and the group-NH_2 of the lateral lysine chain in position 119 in the H2A histone and in position 120 in the H2B histone (see col. 1, lines 57-64). Furthermore, PCT Rules do not permit multiple methods. Therefore, the technical feature linking the inventions of groups I-XIX does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The special technical feature of group I is considered to be a conjugate comprising a histone moiety covalently linked to a protein.

The special technical feature of group II is considered to be a conjugate comprising a histone moiety covalently linked to a nucleic acid.

The special technical feature of group III is considered to be a polynucleotide encoding an in-frame polypeptide conjugate, said polypeptide conjugate comprises a histone moiety and a protein-of-interest.

The special technical feature of group IV is considered to be a method of synthesizing a conjugate comprising a histone moiety with a protein, comprising covalently linking a histone moiety with a protein.

The special technical feature of group V is considered to be a method of synthesizing a conjugate comprising a histone moiety with a nucleic acid.

The special technical feature of group VI is considered to be a method of delivering a protein into a cell, comprising contacting the cell with a protein conjugate.

The special technical feature of group VII is considered to be a method of delivering a nucleic acid into a cell, comprising contacting the cell with a conjugate comprising a nucleic acid.

The special technical feature of group VIII is considered to be a method of treating a proliferative disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a proliferative disorder or disease.

The special technical feature of group IX is considered to be a method of treating a genetic disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a genetic disorder or disease.

The special technical feature of group X is considered to be a method of treating a bacterial infection in a subject in need thereof, comprising administering to the subject a therapeutically

effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a bacterial infection.

The special technical feature of group XI is considered to be a method of treating a viral infection in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a protein, which has a therapeutic activity in treating a viral infection.

The special technical feature of group XII is considered to be a method of treating a proliferative disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a proliferative disorder or disease.

The special technical feature of group XIII is considered to be a method of treating a genetic disorder or disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a genetic disorder or disease.

The special technical feature of group XIV is considered to be a method of treating a bacterial infection in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a bacterial infection.

The special technical feature of group XV is considered to be a method of treating a viral infection in a subject in need thereof, comprising administering to the subject a therapeutically

effective amount of a conjugate, wherein the conjugate comprises a macromolecule-of-interest that is a nucleic acid, which has a therapeutic activity in treating a viral infection.

The special technical feature of group XVI is considered to be a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a protein into cells.

The special technical feature of group XVII is considered to be a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a nucleic acid into cells.

The special technical feature of group XVIII is considered to be a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a conjugate of a first macromolecule covalently attached to a second macromolecule, wherein the first macromolecule is a histone moiety, and the second macromolecule is a protein.

The special technical feature of group XIX is considered to be a method of quantitatively determining a nuclear uptake and/or a cytoplasmic uptake of a conjugate of a first macromolecule covalently attached to a second macromolecule, wherein the first macromolecule is a histone moiety, and the second macromolecule is a nucleic acid.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. The technical feature linking the species does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art (see above describing a species peptide conjugate).

The species are as follows: The molecular structure of the conjugate being claimed in each invention. The molecular structure of particular species of the invention, for example, group I is drawn to a conjugate comprising a peptide, so the amino acid sequence for the histone

moiety and the amino acid sequence for the peptide and any other molecule conjugated to the conjugate claimed. For group II, the nucleic acid sequence and the histone moiety sequence along with any other molecule of interest conjugated with the molecular species.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The technical feature linking the species does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art (see above describing a species peptide conjugate).

5. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim

will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

April 2, 2007

Anand Desai